

Claims

1. A method for screening a first repertoire of members against a second repertoire of members to identify members of the first repertoire which interact with members of the second repertoire, comprising :

(d) providing an array of members of the first repertoire juxtaposed with members of the second repertoire which permits interaction of said first repertoire members with said second repertoire members, said array comprising a solid surface, said first repertoire present on a solid surface in a first series of continuous, non-intersecting lines such that each line of said series comprises a member of said first repertoire, and said second repertoire present on a solid surface in a second series of continuous, non-intersecting lines such that each line of said series comprises a member of said second repertoire, such that members of the first repertoire are juxtaposed to members of the second repertoire; and

(e) detecting an interaction between members of the first and second repertoires, thereby identifying a member of the first repertoire that interacts with a member of the second repertoire.

2. The method according to claim 1, wherein each of said continuous, non-intersecting line of each of said first and second series comprises a different member of said first and second repertoires, respectively.

3. The method according to claim 1 wherein said line comprises a channel, and wherein members of said first and second repertoires placed continuously in said channel, and wherein said channel is cut into a solid material such that each channel containing a member of the first repertoire intersects each channel containing a member of the second repertoire.

4. The method according to claim 1, wherein said first and second series of continuous, non-intersecting lines are present on the same solid support, such that each member of said first repertoire is juxtaposed to each member of said second repertoire.

5. The method according to claim 1, comprising the steps of:

(a) applying said first repertoire to a first solid surface in a first series of continuous, non-intersecting lines such that each line of said series comprises a member of said first repertoire, applying said second repertoire to a second solid surface in a second series of continuous, non-intersecting lines such that each line of said series comprises a member of said second repertoire; and;

(b) juxtaposing the first and second supports such that all members of the first repertoire are juxtaposed with all members of the second repertoire; and

(c) detecting an interaction between the members of the first and second repertoires.

6. A method for screening a first repertoire of members against a second repertoire of members to identify members of the first repertoire which interact with members of the second repertoire, comprising:

(a) providing an array of members of the first repertoire juxtaposed with members of the second repertoire which permits interaction of said first repertoire members with said second repertoire members, said array comprising said first repertoire present in the lumen of a first series of non-intersecting tubes, such that each tube of said series comprises a member of said first repertoire, and further comprising said second repertoire present in the lumen of a second series of non-intersecting tubes, such that each tube of said series comprises a member of said second repertoire, such that the lumen of each of said first series of tubes intersects with the lumen of each of said second series of tubes, such that members of said first repertoire are juxtaposed to members of said second repertoire.

(b) detecting an interaction between members of the first and second repertoires, thereby identifying a member of the first repertoire that interacts with a member of the second repertoire.

7. A method of making an array for screening a first repertoire of members against a second repertoire of members to identify members of the first repertoire which interact with members of the second repertoire comprising:

- (a) providing at least one solid surface;
- (b) depositing on said solid surface a said first repertoire as a series of continuous, non-intersecting lines, such that each of said first series of continuous, non-intersecting lines comprises a member of said first repertoire;
- (c) depositing on said solid surface said second repertoire as a series of continuous, non-intersecting lines, such that each of said second series of continuous, non-intersecting lines comprises a member of said second repertoire, and such that each of said second series of lines intersects with each of said first series of lines, and said first repertoire of members is juxtaposed to said second repertoire of members.

8. A method for screening first, second, and third repertoires of molecules against each other to identify members of the first, second and third repertoires which interact comprising:

- (a) providing an array of members of first, second, and third repertoires juxtaposed to each other which permits interaction of said first, second and third repertoire members, said array comprising three solid surfaces, a member of said first repertoire present on a first solid surface of said array, a member of said second repertoire present on a second solid surface of said array, and a member of said third repertoire present on a third solid surface of said array, such that each of said first, second, and third solid surfaces of said array intersect, such that members of the first, second and third repertoires are juxtaposed; and
- (b) detecting an interaction between members of the first, second and third repertoires, thereby identifying members of the first, second and third repertoires that interact.

9. The method of claim 7, wherein said array is a cube.

10. A method for screening first, second and third repertoires of members against each other to identify members of the first, second and third repertoires which interact, comprising :

(a) providing an array of members of first, second and third repertoires, juxtaposed to each other which permits interaction of said first, second and third repertoire members, said array comprising a solid surface, said first repertoire present on a solid surface in a first series of continuous, non-intersecting lines such that each line of said series comprises a member of said first repertoire, said second repertoire present on a solid surface in a second series of continuous, non-intersecting lines such that each line of said series comprises a member of said second repertoire, and said third repertoire present on a solid surface in a series of continuous, non-intersecting lines such that each line of said series comprises a member of said third repertoire, and such that members of said first, second and third repertoire is juxtaposed to other members of said first, second, and third repertoires; and

(b) detecting an interaction between members of the first, second and third repertoires, thereby identifying members of the first, second and third repertoires that interact.

11. A method for creating a combinatorial library of two-chain polypeptides, wherein each member of said library comprises one member of a first repertoire of single chain polypeptides and one member of a second repertoire of single chain polypeptides, which method comprises the step of providing an array of members of the first repertoire juxtaposed with the members of the second repertoire which permits interaction of said first repertoire members and said second repertoire members, said array comprising a solid surface wherein said first and second repertoires of single chain polypeptides are present on a solid surface in a first and second series of continuous, non-intersecting lines, respectively, such that each line of said first series intersects with each line of said second series, such that members of the first repertoire are juxtaposed members of the second repertoire, thereby generating two-chain polypeptides at the intersection of said first and second series, thereby creating a combinatorial library of two-chain polypeptides.

12. A method of screening a combinatorial library of two-chain polypeptides for binding to a target molecule, wherein said library is produced by a method comprising providing an array of members of a first repertoire juxtaposed with the members of a second repertoire which permits interaction of said first repertoire members and said second repertoire members, said array comprising a solid surface wherein said first and second repertoires of single chain polypeptides are present on a solid surface in a first and second series of continuous, non-intersecting lines, respectively, such that each line of said first series intersects with each line of said second series, such that members of the first repertoire are juxtaposed members of the second repertoire, thereby generating two-chain polypeptides at the intersection of said first and second series, thereby creating a combinatorial library of two-chain polypeptides, the method comprising the steps of contacting said combinatorial library with said target molecule, and detecting the interaction between the two chain polypeptide and the target molecule.

13. The screening method according to claim 12, wherein the combinatorial library is screened for interactions with more than one target molecule.

14. A method for creating a combinatorial library of three chain polypeptides wherein each member of said library comprises one member of a first repertoire of single chain polypeptides, one member of a second repertoire of single chain polypeptide, and one member of a third repertoire of single chain polypeptides, which method comprises the step of providing an array of members of first, second, and third repertoires juxtaposed to each other which permits interaction of said first, second and third repertoire members, said array comprising three solid surfaces, a member of said first repertoire present on a first solid surface of said array, a member of said second repertoire present on a second solid surface of said array, and a member of said third repertoire present on a third solid surface of said array, such that each of said first, second, and third solid surfaces of said array intersect, such that members of the first, second and third repertoires are juxtaposed, thereby generating three-chain polypeptides at the intersection of said first, second, and third solid surfaces, thereby creating a combinatorial library of three-chain polypeptides.

15. A method of screening a combinatorial library of three-chain polypeptides for binding to a target molecule, wherein said library is produced by a method comprising providing an array of members of first, second, and third repertoires juxtaposed to each other which permits interaction of said first, second and third repertoire members, said array comprising three solid surfaces, a member of said first repertoire present on a first solid surface of said array, a member of said second repertoire present on a second solid surface of said array, and a member of said third repertoire present on a third solid surface of said array, such that each of said first, second, and third solid surfaces of said array intersect, such that members of the first, second and third repertoires are juxtaposed, thereby generating three-chain polypeptides at the intersection of said first, second, and third solid surfaces, thereby creating a combinatorial library of three-chain polypeptides, the method comprising the steps of contacting said combinatorial library with said target molecule, and detecting the interaction between the three chain polypeptides and the target molecule.

16. The method of claim 14 or 15, wherein said combinatorial library is screened for interactions with more than one target molecule.

17. A method for creating a combinatorial library of three-chain polypeptides, wherein each member of said library comprises one member of a first repertoire of single chain polypeptides, one member of a second repertoire of single chain polypeptides, and one member of a third repertoire of single chain polypeptides, which method comprises the step of providing an array, comprising a solid surface, wherein the first, second, and third repertoires of single chain polypeptides are present on a solid surface in a first, second, and third series of continuous, non-intersecting lines, respectively, such that each line of said first series intersects with each line of said second and third series, each line of said second series intersects with each line of said first and third series, and each line of said third series intersects with said first and second series, such that members of the first, second and third repertoires are juxtaposed to each other, thereby generating three-chain polypeptides at the intersection of said first, second, and third series, thereby creating a combinatorial library of three-chain polypeptides.

18. A method of screening a combinatorial library of three-chain polypeptides for binding to a target molecule, wherein said library is produced by a method comprising providing an array, comprising a solid surface, wherein a first, second, and third repertoire of single chain polypeptides are present on a solid surface in a first, second, and third series of continuous, non-intersecting lines, respectively, such that each line of said first series intersects with each line of said second and third series, each line of said second series intersects with each line of said first and third series, and each line of said third series intersects with said first and second series, such that members of the first, second and third repertoires are juxtaposed to each other, thereby generating three-chain polypeptides at the intersection of said first, second, and third series, thereby creating a combinatorial library of three-chain polypeptides, the method comprising the steps of contacting said combinatorial library with said target molecule, and detecting the interaction between the three chain polypeptides and the target molecule.

19. The screening method according to claim 17 or 18, wherein the combinatorial library is screened for interactions with more than one target molecule.

20. The method according to claim 1, whereby one or both of the first or second repertoires comprises a plurality of nucleic acid molecules which are expressed to produce their corresponding polypeptides *in situ* in the array.

21. The method according to claim 8 or 10, whereby one or all of the first, second and third repertoires comprises a plurality of nucleic acid molecules which are expressed to produce their corresponding polypeptides *in situ* in the array.

22. The method according to claim 20 or 21, wherein the nucleic acid molecules are in the form of expression vectors which encode polypeptide members of the repertoire, operatively linked to control sequences sufficient to direct the transcription of the nucleic acid molecules.

23. The method according to claim 22, wherein the expression vector is a bacteriophage.

24. The method according to claim 22, wherein the expression vector is a plasmid.

25. The method according to claim 22, wherein the expression vector is a linear nucleic acid molecule.

26. The method according to claim 22, wherein the nucleic acids are contained and expressed within cells.

27. The method according to claim 26, wherein the cells are selected from the group consisting of prokaryotic and eukaryotic cells.

28. The method according to claim 1 or 10, wherein the members of at least one repertoire are arranged in said series of continuous, non-intersecting lines using robotic means.

29. A method for screening a first repertoire of members against a second repertoire of members to identify members of the first repertoire which interact with members of the second repertoire, comprising :

(a) providing an array of members of the first repertoire juxtaposed with members of the second repertoire which permits interaction of said first repertoire members with said second repertoire members, said array comprising a solid surface, said first repertoire present on a solid surface in a first series of continuous, non-intersecting lines such that each line of said series comprises a member of said first repertoire, and said second repertoire present on a solid surface in a second series of continuous, non-intersecting lines such that each line of said series comprises a member of said second repertoire, such that members of the first repertoire are juxtaposed to members of the second repertoire; and

(b) detecting the lack of an interaction between members of the first and second repertoires, thereby identifying members of the first repertoire that do not interact with members of the second repertoire.

30. A method for screening a first repertoire of members against a second repertoire of members to identify members of the first and second repertoires whose interactions with one another are dependent on the presence or absence of a one or more third molecules, comprising:

(a) providing an array of members of the first repertoire juxtaposed with members of the second repertoire which permits interaction of said first repertoire members with said second repertoire members, said array comprising a solid surface, wherein said first repertoire is present on a solid surface in a first series of continuous, non-intersecting lines such that each line of said series comprises a member of said first repertoire, and said second repertoire is present on a solid surface in a second series of continuous, non-intersecting lines such that each line of said series comprises a member of said second repertoire, such that members of the first repertoire are juxtaposed to members of the second repertoire; and

(b) contacting said first and second repertoires with said one or more third molecules;

(c) detecting interactions between members of the first repertoire and members of the second repertoire in the presence of the one or more third molecules, such that members of the first and second repertoires whose interactions with one another are dependent on the presence or absence of the one or more third molecules are identified.

31. The method of claim 30, wherein said first and second repertoires together are contacted with different concentrations of said one or more third molecules.

32. The method according to claim 30, wherein the interaction of the one or more third molecules with one or more members of the first repertoire permits such members of the first repertoire to interact with one or more members of the second repertoire.

33. The method according to claim 30, wherein the interactions between the members of the first and second repertoire require the simultaneous binding of these members to the one or more molecules.

34. The method according to claim 30 wherein the interactions between the members of the first and second repertoire are enhanced by the presence of the one or more third molecules.

35. The method according to claim 30, wherein the interactions between the members of the first and second repertoire are blocked by the presence of the one or more third

molecules.

36. The method according to claim 30, wherein the first and second repertoires are dispensed by a plurality of dispensing events to form the array, and wherein fewer dispensing events are required than the number of interactions to be screened.

37. The method according to claim 36 wherein members of both the first repertoire and the second repertoire are dispensed by a plurality of dispensing events into two or more series of continuous, non-intersecting lines, respectively, each line comprising a member of the first or second repertoires such that the series of lines corresponding to the first repertoire and the series of lines corresponding to the second repertoire intersect such that the number of intersections is greater than the number of dispensing events.

38. A method for determining conditions for a biological interaction, which method comprises creating two or more different sets of variable parameters at the intersections of two or more different sets of intersecting lines, and assaying one or more intersections for a biological interaction, thereby determining the conditions for the biological interaction.

39. A method according to claim 38, wherein the variable parameters are selected from the group consisting of: a buffer composition, a substrate concentration, pH, temperature, the presence of denaturants and the presence of renaturants.

40. A method for screening a first and a second repertoire of enzymes to identify members of the first repertoire and members of the second repertoire which together participate in a two or more step enzymatic reaction that generates a product from a substrate, which method comprises:

(a) providing an array of members of the first repertoire juxtaposed with members of the second repertoire which permits interaction of said first repertoire members and said second repertoire members, said array comprising a solid surface, said first repertoire present on a solid surface in a first series of continuous, non-intersecting lines such that each line of said series comprises a member of said first repertoire, and said second repertoire present on a solid surface in a second series of continuous, non-intersecting lines such that each line of

said series comprises a member of said second repertoire, such that members of the first repertoire are juxtaposed to members of the second repertoire;

(b) contacting said array with said substrate; and

(c) detecting the formation of the product at the intersections of the members of the first and second repertoires, thereby identifying members of the first and second repertoires which together participate in a two or more step enzymatic reaction that creates the product from the substrate.

41. A method for screening a first repertoire of cellular populations against a second repertoire of viral populations to identify viral populations among the repertoire of viral populations that infect cellular populations among the repertoire of cellular populations, which method comprises:

(a) providing an array of members of the first repertoire juxtaposed with members of the second repertoire which permits interaction of said first repertoire members with said second repertoire members, said array comprising a solid surface, wherein said repertoire of cellular populations is present on a solid surface in a first series of continuous, non-intersecting lines such that each line of said series comprises a member of said repertoire of cellular populations, and said repertoire of viral populations is present on a solid surface in a second series of continuous, non-intersecting lines such that each line of said series comprises a member of said repertoire of viral populations, such that each of said first series of lines intersects with each of said second series of lines, such that members of the repertoire of cellular populations are juxtaposed to members of the repertoire of viral populations which permits interaction of said repertoire of cellular populations and said repertoire of said viral populations; and

(b) detecting viral infection in the plurality of cellular populations, thereby identifying viral populations among the repertoire of viral populations that infect cellular populations among the repertoire of cellular populations.

42. A method for screening a plurality of different cellular fractions against one another to identify cellular fractions of said plurality that contain components which interact with components in other cellular fractions of said plurality, which method comprises:

(a) providing an array, comprising a solid surface, comprising a first repertoire of cellular fractions and a second repertoire of cellular fractions wherein said first repertoire is present on a solid surface in a first series of continuous, non-intersecting lines such that each line of said series comprises an individual cell fraction of said first repertoire, and said second repertoire is present on a solid surface in a second series of continuous, non-intersecting lines such that each line of said series comprises an individual cell fraction of said second repertoire, such that each of said first series of lines intersects with each of said second series of lines, such that cell fractions of the first repertoire are juxtaposed to cell fractions of the second repertoire which permits interaction of said first and second repertoire cellular fractions; and

(b) detecting the interaction of different cellular fractions at sites where the different cellular fractions are juxtaposed, thereby identifying cellular fractions of said plurality that contain components which interact with components in other cellular fractions of said plurality.

43. A method for screening a plurality of different cellular populations against one another to identify cellular populations of said plurality that interact with other cellular populations of said plurality, which method comprises:

(a) providing an array, comprising a solid surface, comprising a first repertoire of cellular populations and a second repertoire of cellular populations wherein said first repertoire is present on a solid surface in a first series of continuous, non-intersecting lines such that each line of said series comprises an individual cell population of said first repertoire, and said second repertoire is present on a solid surface in a second series of continuous, non-intersecting lines such that each line of said series comprises an individual cell population of said second repertoire, such that each of said first series of lines intersects with each of said second series of lines, such that cell populations of the first repertoire are

juxtaposed to cell populations of the second repertoire which permits interaction of said first and second repertoire cellular populations; and

(b) detecting the interaction of different cellular populations at sites where the different cellular populations are juxtaposed, thereby identifying cellular populations of said plurality that interact with other cellular populations of said plurality.

44. A method for screening each member of a polypeptide repertoire against each other member of said polypeptide repertoire, in order to identify members of the polypeptide repertoire that interact with other members of the polypeptide repertoire, which method comprises:

(a) providing an array, comprising a solid surface, comprising a first repertoire of polypeptides and a second repertoire of the same polypeptides wherein said first repertoire is present on a solid surface in a first series of continuous, non-intersecting lines such that each line of said series comprises a member of said first repertoire, and said second repertoire is present on a solid surface in a second series of continuous, non-intersecting lines such that each line of said series comprises a member of said second repertoire, such that each of said first series of lines intersects with each of said second series of lines, such that polypeptides of the first repertoire are juxtaposed to polypeptides of the second repertoire which permits interaction of said first and second repertoire polypeptides; and

(b) detecting the interaction of different members of the polypeptide repertoire at sites where the different members are juxtaposed, thereby identifying members of the polypeptide repertoire that interact with other members of the polypeptide repertoire.

45. The method according to claim 1 or 44, which method uses a yeast two-hybrid system to identify those members of the repertoires of molecules that interact with one another.

46. A method for creating a combinatorial library comprising members of a first repertoire of polypeptides paired with members of a second repertoire of polypeptides, which method comprises:

(a) providing an array comprising a solid surface wherein a plurality of host cells

comprising a plurality of nucleotide sequences encoding a first repertoire of polypeptide members is present on a solid surface in a first series of continuous, non-intersecting lines such that each line of said series comprises a member of said first repertoire of polypeptide members, and a plurality of nucleotide sequences encoding a second repertoire of polypeptide members is present on a solid surface in a second series of continuous, non-intersecting lines such that each line of said series comprises a member of said second repertoire of polypeptide sequences of to create an array, such that each of said first series of lines intersects with each of said second series; and

(b) transforming the cells containing the nucleotide members of the first repertoire with the nucleotide sequences that encode the members of the second repertoire where the two repertoires intersect; and

(c) expressing the nucleotide sequences to produce the corresponding polypeptides of the first and second repertoires; thereby creating a combinatorial library consisting of members of the first repertoire of polypeptides paired with members of the second repertoire of polypeptides.

47. A method for screening the combinatorial library for members of a first repertoire of polypeptides that interact with members of a second repertoire of polypeptides, wherein said combinatorial library is generated by a method comprising providing an array comprising a solid surface and a plurality of host cells comprising a plurality of nucleotide sequences encoding the first repertoire of polypeptide members present on a solid surface in a first series of continuous, non-intersecting lines such that each line of said series comprises a member of said first repertoire of polypeptide members, and a plurality of nucleotide sequences encoding the second repertoire of polypeptide members present on a solid surface in a second series of continuous, non-intersecting lines such that each line of said series comprises a member of said second repertoire of polypeptide sequences of to create an array, such that each of said first series of lines intersects with each of said second series; transforming the cells containing the nucleotide members of the first repertoire with the nucleotide sequences that encode the members of the second repertoire where the two repertoires intersect; and expressing the nucleotide sequences to produce the corresponding

polypeptides of the first and second repertoires; thereby creating a combinatorial library consisting of members of the first repertoire of polypeptides paired with members of the second repertoire of polypeptides, the method comprising the step of detecting an interaction between the polypeptide members of the first and second repertoires, thereby identifying members of the first repertoire that interact with members of the second repertoire.

48. A method for creating a combinatorial library consisting of members of a first repertoire of polypeptides paired with members of a second repertoire of polypeptides, which method comprises:

- (a) providing an array comprising a solid surface and a plurality of host cells comprising a plurality of nucleotide sequences encoding a first repertoire of polypeptide members present on a solid surface in a first series of continuous, non-intersecting lines such that each line of said series comprises a member of said first repertoire of polypeptide members, and a plurality of viruses containing a plurality of nucleotide sequences encoding a second repertoire of polypeptide members present on a solid surface in a second series of continuous, non-intersecting lines such that each line of said series comprises a member of said second repertoire of polypeptide sequences of to create an array, such that each of said first series of lines intersects with each of said second series;
- (b) infecting the cells containing the nucleotide members encoding the first repertoire with the viruses that contain the nucleotide members encoding the second repertoire where the first and second series of lines intersect; and
- (c) expressing the nucleotide sequences to produce the corresponding polypeptides of the first and second repertoires, thereby creating a combinatorial library consisting of members of the first repertoire of polypeptides paired with members of the second repertoire of polypeptides.

49. A method of screening the combinatorial library to identify members of a first repertoire of polypeptides that interact with members of a second repertoire of polypeptides, wherein said combinatorial library is generated by the method comprising providing an array comprising a solid surface and a plurality of host cells comprising a plurality of nucleotide

sequences encoding the first repertoire of polypeptide members present on a solid surface in a first series of continuous, non-intersecting lines such that each line of said series comprises a member of said first repertoire of polypeptide members, and a plurality of viruses containing a plurality of nucleotide sequences encoding the second repertoire of polypeptide members present on a solid surface in a second series of continuous, non-intersecting lines such that each line of said series comprises a member of said second repertoire of polypeptide sequences of to create an array, such that each of said first series of lines intersects with each of said second series; infecting the cells containing the nucleotide members encoding the first repertoire with the viruses that contain the nucleotide members encoding the second repertoire where the first and second series of lines intersect; and expressing the nucleotide sequences to produce the corresponding polypeptides of the first and second repertoires, thereby creating a combinatorial library consisting of members of the first repertoire of polypeptides paired with members of the second repertoire of polypeptides, the method comprising the step of detecting an interaction between polypeptide members of the first and second repertoires, whereby members of the first repertoire that interact with members of the second repertoire are identified.

50. A method for creating a yeast two hybrid library consisting of members of a first repertoire of polypeptides paired with members of a second repertoire of polypeptides, which method comprises:

(a) providing an array comprising a solid surface and a first plurality of yeast cells comprising a plurality of nucleotide sequences encoding a first repertoire of polypeptide members present on a solid surface in a first series of continuous, non-intersecting lines such that each line of said series comprises a member of said first repertoire of polypeptide members, and a second plurality of yeast cells containing a plurality of nucleotide sequences encoding a second repertoire of polypeptide members present on a solid surface in a second series of continuous, non-intersecting lines such that each line of said series comprises a member of said second repertoire of polypeptide sequences of to create an array, such that each of said first series of lines intersects with each of said second series;

(b) allowing the yeast cells containing the members of the first repertoire to mate

with the yeast cells containing the members of the second repertoire where the two repertoires intersect; and

(c) expressing the nucleotide sequences to produce the corresponding polypeptides of the first and second repertoires, thereby creating a yeast two hybrid library comprising members of a first repertoire of polypeptides paired with members of a second repertoire of polypeptides.

51. A method of screening a combinatorial library to identify members of a first repertoire of polypeptides that interact with members of a second repertoire of polypeptides, wherein said combinatorial library is generated by the method comprising providing an array comprising a solid surface and a first plurality of yeast cells comprising a plurality of nucleotide sequences encoding the first repertoire of polypeptide members present on a solid surface in a first series of continuous, non-intersecting lines such that each line of said series comprises a member of said first repertoire of polypeptide members, and a second plurality of yeast cells containing a plurality of nucleotide sequences encoding the second repertoire of polypeptide members present on a solid surface in a second series of continuous, non-intersecting lines such that each line of said series comprises a member of said second repertoire of polypeptide sequences of to create an array, such that each of said first series of lines intersects with each of said second series; allowing the yeast cells containing the members of the first repertoire to mate with the yeast cells containing the members of the second repertoire where the two repertoires intersect; and expressing the nucleotide sequences to produce the corresponding polypeptides of the first and second repertoires, thereby creating a yeast two hybrid library comprising members of the first repertoire of polypeptides paired with members of the second repertoire of polypeptides, the method comprising the step of detecting an interaction between the polypeptide members of the first and second repertoires, whereby members of the first repertoire that interact with members of the second repertoire are identified.

52. A method of creating a combinatorial chemical library comprising:

- (a) providing an array comprising a solid surface and a first repertoire of chemical groups comprising a first reactive group present on said solid surface in a first series of continuous, non-intersecting lines;
- (b) reacting said solid surface with a reagent to modify said first reactive group to render said first reactive group capable of forming a chemical bond with a second reactive group;
- (c) depositing a second repertoire on said solid surface comprising a second reactive group capable of forming a chemical bond with said first reactive group, wherein said second repertoire is deposited in a second series of continuous, non-intersecting lines, such that each line of said first series intersects with each line of said second series, such that each member of said first repertoire is juxtaposed to each member of said second repertoire, wherein a reactive group of said second repertoire forms a chemical bond with a reactive group of said second repertoire thereby producing a combinatorial chemical library.

53. A method for screening a first repertoire comprising a combinatorial chemical library against a repertoire of members to identify members of the first repertoire which interact with members of the second repertoire, wherein said combinatorial chemical library is produced by a method comprising providing an array comprising a solid surface and a first repertoire of chemical groups comprising a first reactive group present on said solid surface in a first series of continuous, non-intersecting lines; reacting said solid surface with a reagent to modify said first reactive group to render said first reactive group capable of forming a chemical bond with a second reactive group; depositing a second repertoire on said solid surface comprising a second reactive group capable of forming a chemical bond with said first reactive group, wherein said second repertoire is deposited in a second series of continuous, non-intersecting lines, such that each line of said first series intersects with each line of said second series, such that each member of said first repertoire is juxtaposed to each member of said second repertoire, wherein a reactive group of said second repertoire forms a chemical bond with a reactive group of said second repertoire thereby producing a

combinatorial chemical library, the method comprising the step of juxtaposing said combinatorial chemical library to said second repertoire and detecting an interaction between members of said combinatorial library and members of said second repertoire, thereby identifying members of said first repertoire comprising said combinatorial library which interact with members of said second repertoire.